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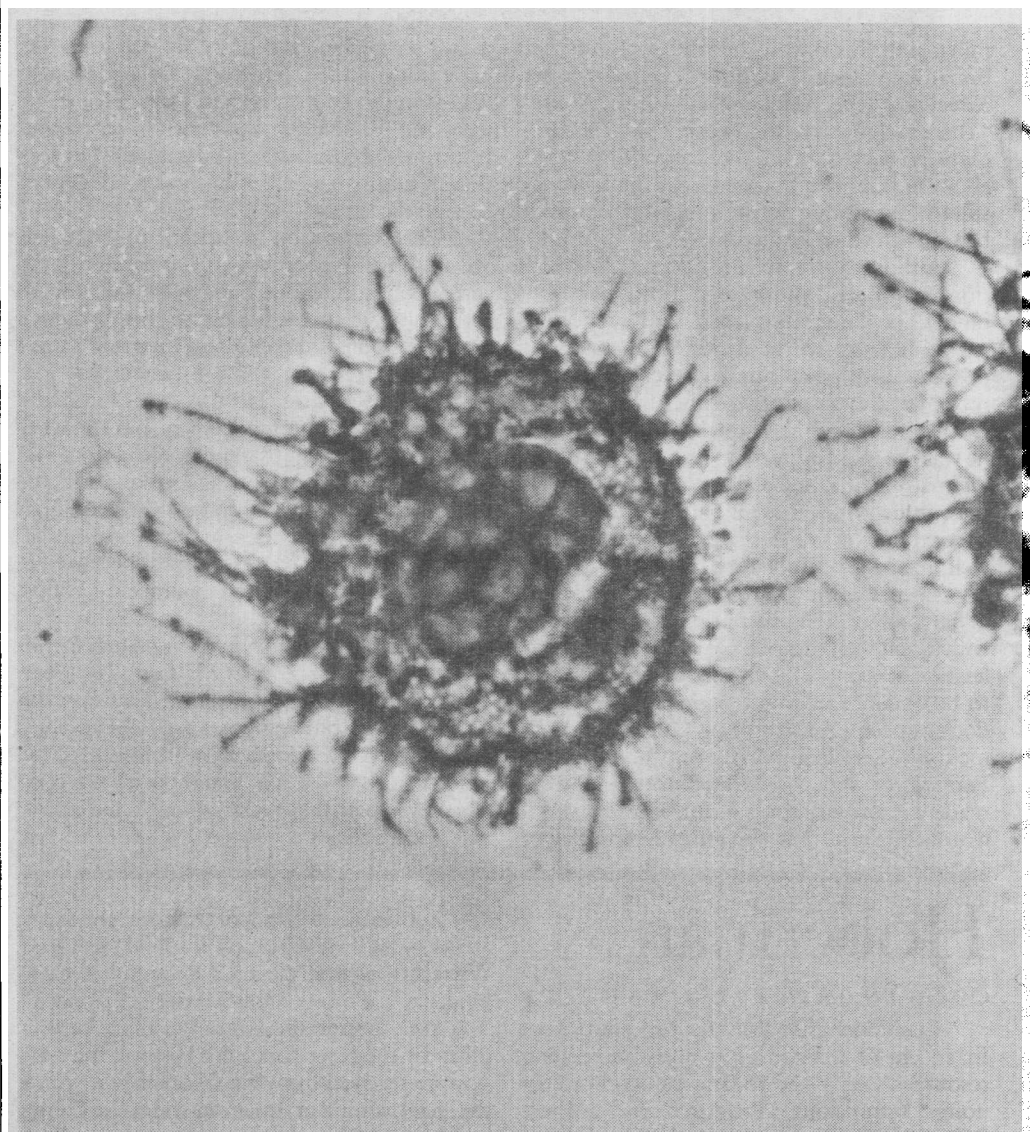
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Dendritic cells are found in the lining of the vagina and foreskin. Can one type of HIV infect them more efficiently than others?

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# Not So Fast

## Hopeful New AIDS Findings May Lead to Dangerous Delusions

By Mark Schoofs

**T**he hottest ticket in Washington this week isn't to an inaugural ball. It's to the 4th Conference on

Retroviruses and Opportunistic Infections, the most prestigious annual AIDS science meeting.

The 2300 lucky participants (hundreds more were turned away) will learn more about how patients are faring on the widely heralded new protease-inhibitor drugs. But other key findings will be presented. New research will cast doubt on an earlier, widely publicized claim that there is a "heterosexual strain" of HIV that can be spread more easily through vaginal intercourse. Other research will suggest that the new drugs make many—but not all—patients less infectious.

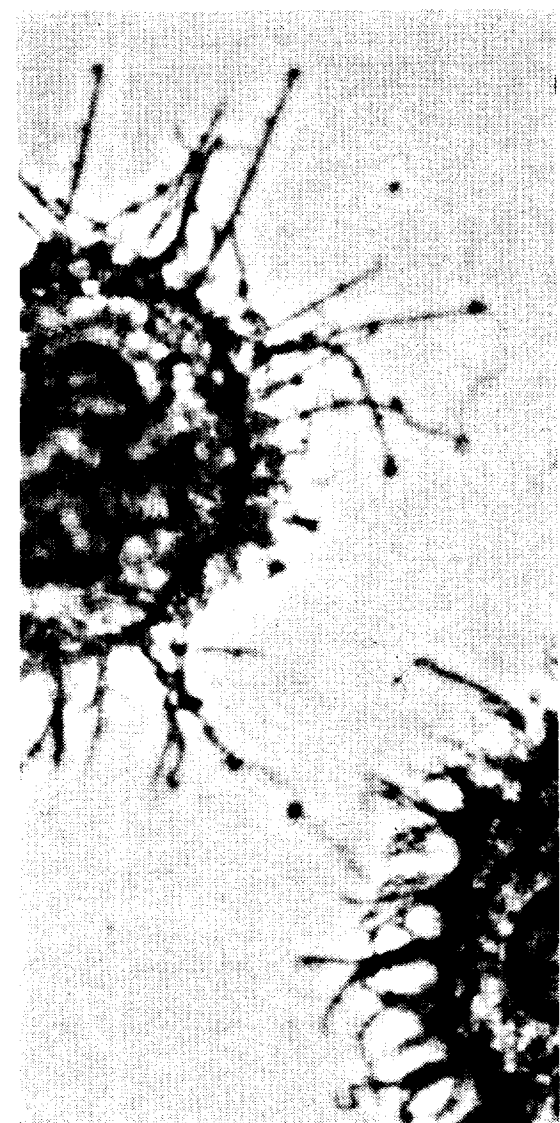
This second finding is sharply double-edged. If it holds up—and if people maintain safer sex—then the number of new infections could drop. But if people believe the danger has

abated, then a rise in unsafe practices could overwhelm any decrease in infectiousness—and more people could actually get HIV.

**O**ne of the great mysteries of heterosexual AIDS unfolded in Thailand, where, around 1986, an epidemic sprang up among IV-drug users. Then, in 1989, HIV exploded among non-drug-using heterosexuals. Intriguingly, scientists discovered that the epidemic among IV-drug users was caused by a different strain of HIV than the epidemic among heterosexuals.

Scientists have classified HIV into 10 "subtypes," labeled A through J. The IV-drug users were infected with subtype B, which predominates in North America and Europe; the heterosexuals were almost all infected with subtype E. Why hadn't B, which had a three-year head start, sparked a heterosexual epidemic? After all, IV-drug users have sex, too.

Many social factors influence the course of epidemics, but scientists wondered whether an explanation lay in the difference between the



MELISSA POPE/COURTESY ROCKEFELLER UNIVERSITY

Could these other cells have "contaminated" Essex's experiments? Pope thinks that might be the case, but Essex basically dismisses this possibility. In turn, he questions Pope's work by pointing to other research showing HIV can, in fact, replicate in dendritic cells.

On such details hang great scientific mysteries—and heated debate. Meanwhile, the riddle of the Thai epidemic remains unsolved.

**B**ruce Patterson runs the AIDS hotline for Gay Men's Health Crisis, and these days, he says, "Some callers are making great leaps of logic." People have heard that the new protease inhibitors can reduce the amount of HIV in a person's blood so dramatically that scientists can't detect it. "Doesn't it therefore follow that I'm not infectious?" Patterson says his callers ask. "We've had calls from women whose boyfriends or husbands are positive and they think they can have a baby without it getting infected. And some people have gone so far as to say, I really don't need to wear condoms anymore, do I? It's scary that people would be making those assumptions."

Scary indeed, but new data might fuel those notions. When examining blood or semen, scientists can look for HIV that is inside cells—called "provirus"—or for "free virus" that is floating in semen or blood. Two separate research teams—one from Boston and the other from New York's Aaron Diamond AIDS Research Center—have found that the amount of free virus in semen generally falls sharply when combination therapy is effective in suppressing HIV in the blood. But the level of free virus in the semen of one Boston patient actually *increased* after he started taking the drugs.

Even if the amount of free virus dropped to zero, a patient could still be infectious. In fact, among patients from both studies, many harbored HIV inside cells in their ejaculate, *even when the standard test used by most doctors couldn't detect HIV in their blood*. Could this "provirus" infect someone? "Sure," says David Ho, a leading AIDS scientist who heads the Aaron Diamond Center.

There are other dangers: The drugs will not work on all people, or they may only work for a short while. If the therapy does fail, it may mean the patient has developed a drug-resistant strain of HIV, rendering himself and anyone he infects harder—perhaps even impossible—to treat. Then, too, HIV levels can fluctuate "from month to month," says Kenneth Mayer, a veteran researcher who worked on the Boston study. (Indeed, both studies are small and haven't followed patients for very long.) And Ho, citing technical limitations, says, "Even if we haven't detected anything infectious, it might be there."

There is some hope that these caveats might be getting through. Reginald Miller, codirector of education for the

Minority Task Force on AIDS, has heard the same questions that are coming into GMHC's hotline. But, he says, "Most of the people I see are very skeptical. They recognize that there may be virus present but we can't measure it."

But there will surely be many people who desperately want to believe that the danger of infection has passed. Here's how Patterson would counsel these callers: "I can understand you wanting to stop using condoms with your boyfriend. But how are you going to feel about infecting him if you could have prevented it?" ♦

Conference abstracts and proceedings are available on the Internet, [www.retroconference.org](http://www.retroconference.org).

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two strains of virus. Then Max Essex, chair of the Harvard AIDS Institute, found that subtype E is better than B at replicating in cells lining the vagina and foreskin, called Langerhans or dendritic cells. In other words, E seemed to be better adapted to infecting the cells it was most likely to encounter during vaginal sex, which made the press trumpet a "heterosexual strain" of HIV.

But now, researchers at two different laboratories—Rockefeller University here in New York, and the U.S. Army—have been unable to duplicate Essex's findings. These teams found no difference in the ability of B and E viruses to infect dendritic cells. Does this undermine the claim that E is more easily spread by sex than B? "Yes, I think so," replies Rockefeller researcher Melissa Pope.

Not at all, insists Essex. And while the new findings are certainly not good news for his work, the jury is still

out. Why? Because the researchers used slightly different methods to carry out their experiments, and those might have affected the outcome. For example, Essex looked only at cells lying on the surface of the vaginal lining; the Rockefeller and army teams looked at cells from the surface and a bit deeper down. Army researcher Sarah Frankel acknowledges that this could account for the different findings, though she thinks that's "unlikely."

Many factors—which scientists are only beginning to unravel—influence HIV's ability to infect cells. Indeed, the Rockefeller team found that HIV was able to enter dendritic cells but, once inside them, was not able to replicate and produce viral offspring. However, when dendritic cells were mixed with another kind of cell, then HIV was able to replicate.

**'Some people have gone so far as to say, I really don't need to wear condoms anymore, do I? It's scary.'**

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